

**DETAILED ACTION**

**EXAMINER'S AMENDMENT**

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Michelle Shannon on 14 May 2004.

The application has been amended as follows:

Please cancel claims 89-95, 98-104, 214, 215, 223, 224, 275-278, 287, 288, 294, 295, 309, 310, 316, 317, 331, 332, 338, and 339.

Please amend claims 212, 213, 221, 222, 230, 285, 286, 292, 293, 307, 308, 314, 315, 328-330, 336 and 337 as follows.

*27 212.* (Currently Amended) A method of stimulating B lymphocyte proliferation, differentiation or survival comprising administering to an individual, an effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates B lymphocyte proliferation, differentiation, or survival comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;
- (b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the protein having said amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

~~28~~ <sup>27</sup> ~~213~~. (Currently Amended) The method of claim ~~212~~ wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence. comprises amino acid sequence (a).

~~32~~ <sup>32</sup> ~~21~~. (Currently Amended) A method of stimulating B lymphocyte proliferation, differentiation or survival comprising administering to an individual, an effective amount of a protein comprising a first amino acid sequence that is 90%95% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates B lymphocyte proliferation, differentiation, or survival selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the protein having said first amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

~~33~~ <sup>32</sup> ~~22~~. (Currently Amended) The method of claim ~~221~~ wherein the protein comprises a first amino acid sequence which is 95% or more identical to said second amino acid sequence amino acid sequence (a).

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~~37~~ <sup>280</sup>. (Currently Amended) A method of stimulating B lymphocyte proliferation, differentiation or survival comprising administering to an individual, [[a]] an effective amount of a protein consisting of an amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

~~45~~ <sup>285</sup>. (Currently Amended) A method of stimulating B lymphocyte proliferation, differentiation or survival comprising contacting B lymphocytes with an effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates B lymphocyte proliferation, differentiation, or survival comprising an amino acid sequence selected from the group consisting of:

~~(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;~~

~~(b) — the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and~~

~~(c) — the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;~~

~~wherein the protein having said amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

~~46~~ <sup>286</sup>. (Currently Amended) The method of claim <sup>45</sup> ~~285~~ wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence comprises amino acid sequence (a).

~~50~~ <sup>292</sup>. (Currently Amended) A method of stimulating B lymphocyte proliferation, differentiation or survival comprising contacting B lymphocytes with an effective amount of a protein comprising a first amino acid sequence that is 90% 95% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates B lymphocyte proliferation, differentiation, or survival selected from the group consisting of:

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(d) ~~the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;~~

(e) ~~the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and~~

(f) ~~the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;~~

~~wherein the protein having said first amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

51 293. (Currently Amended) The method of claim <sup>50</sup> ~~292~~ wherein the protein comprises a first amino acid sequence which is 95% or more identical to said second amino acid sequence amino acid sequence (a).

63 307. (Currently Amended) A method of stimulating T lymphocyte proliferation or differentiation comprising administering to an individual, an effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates T lymphocyte proliferation or differentiation comprising an amino acid sequence selected from the group consisting of.

(g) ~~the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;~~

(h) ~~the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and~~

(i) ~~the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;~~

~~wherein the protein having said amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.~~

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*64* 308. (Currently Amended) The method of claim 307 wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence comprises amino acid sequence (a).

*68* 314. (Currently Amended) A method of stimulating T lymphocyte proliferation or differentiation comprising administering to an individual, an effective amount of a protein comprising a first amino acid sequence that is 90%95% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates T lymphocyte proliferation or differentiation selected from the group consisting of:

(j) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(k) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(l) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the protein having said first amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

*69* 315. (Currently Amended) The method of claim 314 wherein the protein comprises a first amino acid sequence which is 95% or more identical to said second amino acid sequence amino acid sequence (a).

*80* 328. (Currently Amended) The method of claim 325 327 wherein said protein is labeled.

*81* 329. (Currently Amended) A method of stimulating T lymphocyte proliferation or differentiation comprising contacting T lymphocytes with an effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein

having said first amino acid sequence stimulates T lymphocyte proliferation or differentiation comprising an amino acid sequence selected from the group consisting of:

(m) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(n) — the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(o) — the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the protein having said amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

8.2 330. (Currently Amended) The method of claim 329 wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence comprises amino acid sequence (a).

8.6 336. (Currently Amended) A method of stimulating T lymphocyte proliferation or differentiation comprising contacting T lymphocytes with an effective amount of a protein comprising a first amino acid sequence that is 90%95% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the protein having said first amino acid sequence stimulates T lymphocyte proliferation, proliferation or differentiation selected from the group consisting of:

(p) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(q) — the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(r) — the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the protein having said first amino acid sequence can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

337. (Currently Amended) The method of claim 336 wherein the protein comprises a first amino acid sequence which is 95% or more identical to said second amino acid sequence amino acid sequence (a).

*Informal Examiner's Amendment*

2. At pg 22, line 1, of the specification, paragraph [0066], the Examiner has amended the specification to indicate that the neutrokinin-alpha amino acid sequence shown in Figures 7A-1 to 7A-2 is SEQ ID NO: 2. (Support can be found throughout the specification.)

*Conclusion*

The Examiner's amendment to the claims served to clarify the claims. Applicant has the right to file divisional or continuation applications to protect the inventions in the cancelled claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

102. (Previously Presented) The method of claim 98 wherein the protein also comprises a heterologous amino acid sequence.

103. (Previously Presented) The method of claim 102 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

104. (Previously Presented) The method of claim 98 wherein said protein is labeled.

105-106. (Cancelled)

1 107. (Previously Presented) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein consisting of the amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

2 108. (Previously Presented) The method of claim 107 wherein the protein is fused to a heterologous amino acid sequence.

3 109. (Previously Presented) The method of claim 108 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

4 110. (Previously Presented) The method of claim 107 wherein said protein is labeled.

111-112. (Cancelled)

7 113. (Previously Presented) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein comprising the amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

8 ~~114~~. (Previously Presented) The method of claim ~~113~~ <sup>7</sup> wherein the protein also comprises a heterologous amino acid sequence.

9 ~~115~~. (Previously Presented) The method of claim ~~114~~ <sup>8</sup> wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

10 ~~116~~. (Previously Presented) The method of claim ~~113~~ <sup>7</sup> wherein said protein is labeled.

117-118. (Cancelled)

11 ~~119~~. (Previously Presented) The method of claim ~~113~~ <sup>7</sup> wherein the immunodeficiency is common variable immunodeficiency (CVID).

120. (Cancelled)

12 ~~121~~. (Previously Presented) The method of claim ~~113~~ <sup>7</sup> wherein the immunodeficiency is Selective IgA deficiency.

122-125. (Cancelled)

13 ~~126~~. (Currently Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the polypeptide protein having said first amino acid sequence modulates stimulates B lymphocyte proliferation, differentiation, or survival.

14 ~~127~~. (Previously Presented) The method of claim ~~126~~ <sup>13</sup> wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence.